GAU/1648 #19

FULBRIGHT & JAWORSKI L.L.P.
A REGISTERED LIMITED LIABILITY PARTNERSHIP
600 CONGRESS AVENUE, SUITE 2400
AUSTIN, TEXAS 78701

TELEPHONE: 512/474-5201
FACSIMILE: 512/536-4598

STEVEN L. HIGHLANDER
PARTNER

INTERNET ADDRESS:
SHIGHLANDER@FULBRIGHT.COM

DIRECT DIAL: 512/536-3184

HOUSTON
WASHINGTON, D.C.
AUSTIN
SAN ANTONIO
DALLAS
NEW YORK
LOS ANGELES
MINNEAPOLIS
LONDON
HONG KONG

February 6, 2002

FILE: INRP:081

COPY OF PAPERS
ORIGINALLY FILED

CERTIFICATE OF MAILING
37 C.F.R 1.8

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231, on the date below:

February 6, 2002 — Date

Steven L. Highlander

Commissioner for Patents
Washington, DC 20231

RE: *SN 09/203,078 "METHOD FOR THE PRODUCTION AND PURIFICATION OF ADENOVIRAL VECTORS" – Shuyuan Zhang et al.*

Sir:

Enclosed for filing in the above-referenced patent application is a Supplemental Information Disclosure Statement, Form PTO-1449, and references (C103).

A fee as set forth in 37 C.F.R. § 1.17(p) in the amount of $180.00 is enclosed herewith. If an appropriate check has not been enclosed, or if it is insufficient, the Commissioner is hereby authorized to deduct any necessary fees from Fulbright & Jaworski L.L.P. Account No.: 50-1212/10012499/SLH.

Please date stamp and return the enclosed postcard evidencing receipt of these materials.

Respectfully submitted,

Steven L. Highlander
Reg. No. 37,642

SLH/cmb
Encl: as noted

C103

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AVENTIS PHARMACEUTICALS PRODUCTS INC. and AVENTIS PHARMA, S.A., Plaintiffs, v. INTROGEN THERAPEUTICS, INC., Defendant.	C.A. No. JURY DEMAND

COMPLAINT

Plaintiffs, AVENTIS PHARMACEUTICALS PRODUCTS INC. and AVENTIS-PHARMA S.A. (collectively "Aventis"), for their complaint against INTROGEN THERAPEUTICS, INC. ("Introgen"), state as follows:

THE PARTIES

1. Plaintiff Aventis Pharmaceuticals Products Inc. is a corporation duly organized and existing under the laws of the state of Pennsylvania, having a principal place of business at Route 202-206 Bridgewater, New Jersey.

2. Plaintiff Aventis Pharma S.A. is a corporation organized and existing under the laws of France, having a principal place of business at 20 Avenue Raymond, Antony, Croix-de-Berny, France.

3. Upon information and belief, Introgen is a corporation organized and existing under the laws of the state of Delaware, having a principal place of business at 301 Congress Avenue, Suite 1850, Austin, Texas 78701.

JURISDICTION AND VENUE

4. By this action, Aventis seeks relief against Introgen pursuant to 35 U.S.C. § 256 on the grounds that Introgen's United States Patent No. 6,194,191 improperly fails to name Aventis inventors, who were omitted from the patent with no deceptive intent on the part of the Aventis inventors. Accordingly, the Court has subject matter jurisdiction over this dispute pursuant to 28 U.S.C. §§ 1331 and 1338(a).

5. Aventis also seeks relief against Introgen on the grounds that Introgen improperly breached the collaboration agreement between the parties by failing to properly maintain confidential information developed and owned by Aventis and disclosed to Introgen by Aventis pursuant to the collaboration agreement. Aventis is the combination of a citizen of a foreign state and a citizen of a state different from the state of Introgen's citizenship. Aventis has suffered damages in excess of $75,000, exclusive of interest and costs, as the direct result of Introgen's wrongful conduct. Accordingly, the Court has jurisdiction over this claim pursuant to 28 U.S.C. § 1332(a)(1). Moreover, the breach of contract claim arises out of the same nucleus of operative facts that underlies the correction of inventorship claim, in that Introgen incorporated the confidential information into the application that issued as U.S. Patent No. 6,194,191. As a result, this Court has supplemental jurisdiction over the breach of contract claim pursuant to 28 U.S.C. § 1367(a).

6. Venue is proper in this district pursuant to 28 U.S.C. § 1391(b), in that defendant Introgen is a Delaware corporation and, thus, resides in this judicial district. This Court has personal jurisdiction over Introgen by virtue of Introgen's presence in this judicial district.

BACKGROUND

7. Adenoviral vectors have been used by researchers to deliver recombinantly-produced genetic material, such as DNA, to evaluate new methods of treating a variety of cancers. The recombinant gene is incorporated into the viral genome, and the virus is used to infect mammalian cells growing in a cell culture vessel. The adenovirus particles infect the mammalian cells and replicate within the mammalian cells, producing more of the modified adenovirus. Typically, the infected mammalian cells are caused to burst, or "lyse," at some point in the growth cycle of the adenovirus, by the addition of a detergent to the cell culture medium, or by alternately freezing and thawing the medium, for example. If allowed to continue through the normal adenoviral growth cycle, the mammalian cells would, at some point, lyse on their own, a process sometimes called autolysis. Lysis, whether induced or autolysis, releases the adenovirus progeny, which may then be purified and used to deliver the modified gene in gene therapy research and/or treatment.

8. On October 7, 1994, Rhône-Poulenc Rorer Pharmaceuticals, Inc. ("RPRP"), a predecessor-in-interest to Aventis Pharmaceuticals Products Inc., entered into a collaboration agreement with Introgen to develop and commercialize novel gene therapy products ("the Agreement").

9. Between November 1994 and March 1995, Francis Blanche and Jean-Marc Guillaume, researchers at Rhône-Poulenc Rorer, S.A. ("RPRSA"), a predecessor-in-interest to Aventis Pharma, S.A., conceived and reduced to practice a method of growing adenovirus involving an "autolysis" technique. The RPRSA researchers discovered that by employing the autolysis technique, the adenovirus could be replicated in submerged

liquid culture, and the adenovirus could be easily purified from the supernatant portion of the cell culture. An important advantage of the RPRSA technique is that it allowed for larger volumes of cell culture medium, and thus allowed larger amounts of adenovirus to be grown in a given batch.

10. In November 1995, within the terms of the Agreement, researchers from RPRSA met with representatives of Introgen, and explained to the Introgen representatives the autolysis technique RPRSA had developed to grow adenovirus. The Introgen representatives explained the conventional technique used by Introgen, involving either a detergent or freeze/thaw lysis step. After discussing the techniques, the parties agreed to conduct a comparative experiment, to investigate the differences between the new RPRSA autolysis technique and the conventional Introgen technique.

11. In furtherance of this comparative experiment, RPRP provided Introgen with the details of the RPRSA autolysis method. Despite this, Introgen was unable to perform the process initially, and on January 7, 1996, Introgen sent a letter to RPRP asking for clarification and details on the RPRSA autolysis method, including the yield achieved with the autolysis method, the relative activity of the adenovirus produced using the autolysis method and the conventional lysis method, and details concerning the new RPRSA autolysis technique. On January 8, 1996, RPRP provided the requested information, and Introgen performed the comparative experiment in February 1996.

12. The Agreement includes a provision requiring that a party receiving confidential information from the other party must maintain that information in secrecy for the term of the Agreement and for five years after the Agreement is terminated. While the Agreement contemplates that a party may use the other party's confidential information

for, among other things, filing and prosecuting patent applications, this provision requires that the party disclosing the confidential information give "reasonable advance notice" to the owner of the confidential information. At no time during the term of the Agreement did Introgen provide any notice to RPRP or Aventis that Introgen intended to disclose the autolysis method in a patent application.

13. Additionally, the Agreement includes a provision specifying that any invention made solely by an RPRP employee would be solely owned by RPRP and any invention made solely by an Introgen employee would be owned solely by Introgen. According to the Agreement, inventions jointly made by RPRP and Introgen employees would be jointly owned.

COUNT I: CORRECTION OF INVENTORSHIP OF U.S. PATENT NO. 6,194,191 PURSUANT TO 35 U.S.C. § 256

14. Aventis realleges and incorporates herein by reference the allegations of the foregoing Paragraphs 7-13.

15. Notwithstanding the provisions of the Agreement relating to ownership of inventions and maintenance of confidential information, on November 20, 1996, Introgen filed a provisional United States Patent application ("the Introgen provisional application") directed to a method for the production and purification of adenoviral vectors. The Introgen provisional application was the first application in a chain of applications leading to the issuance of United States Patent No. 6,194,191 (copy attached as Exhibit A).

16. The Introgen provisional application, like the specification of the '191 patent, includes only a cryptic reference to autolysis as a means of lysing the mammalian cells to

liberate the adenovirus. However, several of the claims of the '191 patent are specifically directed to an autolysis method. For example, claim 1 reads as follows:

> 1. A method for producing a purified adenovirus composition comprising:
> (a) growing host cells in a media;
> (b) providing nutrients to said host cells by perfusion or a fed-batch process;
> (c) infecting said host cells with an adenovirus;
> (d) lysing said host cells to provide a cell lysate comprising adenovirus, wherein said lysis is achieved through autolysis of infected cells; and
> (e) purifying adenovirus from said lysate to provide a purified adenovirus composition.

17. The reference in claim 1 of the '191 patent to autolysis of the infected host cells refers to the work of RPRSA inventors Dr. Blanche and Dr. Guillaume and, therefore, Dr. Blanche and Dr. Guillaume should have been identified, at the very least, as co-inventors on the '191 patent, if not the sole inventors. Thus, Drs. Blanche and Guillaume are entitled to be named on the '191 patent as inventors.

18. Until after the international patent application corresponding to the '191 patent was published, Dr. Blanche and Dr. Guillaume were not aware that Introgen had filed a patent application. It was not until after the '191 patent issued that Dr. Blanche and Dr. Guillaume learned that Introgen succeeded in securing claims directed to their work on the autolysis technique. Accordingly, neither Dr. Blanche nor Dr. Guillaume was involved in any decision to omit their names from the named inventors on the '191 patent and, indeed, this step was taken without their knowledge and consent. Therefore, neither Dr. Blanche nor Dr. Guillaume had any involvement in their being omitted as inventors, much less any deceptive intent in any such omission.

19. Accordingly, Aventis is entitled to an Order directing the Commissioner of the United States Patent and Trademark Office to correct the inventorship of the '191 patent, naming Dr. Francis Blanche and Dr. Jean-Marc Guillaume as inventors.

COUNT II: BREACH OF CONTRACT

20. Aventis realleges and incorporates herein by reference the foregoing paragraphs 7-19.

21. Contrary to the provisions of the Agreement, Introgen incorporated confidential information obtained from RPRP pursuant to the Agreement into the patent application that issued as the '191 patent, thereby publicizing such confidential information upon issuance of the '191 patent. This confidential information pertained to the autolysis technique, discussed above.

22. Introgen failed to provide reasonable advance notice to RPRP or Aventis prior to disclosing the confidential in the Introgen patent applications discussed above. Paragraph 16.2 of the Agreement requires that reasonable advance notice be provided to the owner of the confidential information prior to, *inter alia*, disclosing such confidential information in a patent application.

23. On information and belief, the information pertaining to the autolysis technique does not fall within one of the categories of information excluded as confidential information within the meaning of the Agreement (¶ 16.1(a)-(d)). That is, the information was not already known to Introgen, was not generally available to the public at the time of disclosure to Introgen, did not become generally available to the public other than by Introgen's publication in the '191 patent, was not lawfully disclosed to Introgen by a party other than RPRP, and was not developed independently by Introgen.

24. Introgen has not informed RPRP or Aventis that it considers the autolysis information to be encompassed by one of the categories of Paragraph 16.1 of the Agreement.

25. Aventis has suffered damages as the result of Introgen's breach of the Agreement, and will continue to suffer damages unless and until Introgen is enjoined from further breaching the Agreement.

RELIEF REQUESTED

WHEREFORE, Aventis requests judgment and relief as follows:

(A) a judgment that Dr. Francis Blanche and Dr. Jean-Marc Guillaume are correct and true inventors of the subject matter of United States Patent No. 6,194,191 and an Order directing the Commissioner of the United States Patent and Trademark Office to correct the '191 patent in accordance with such judgment;

(B) a judgment that Introgen has breached the collaboration agreement between the parties by incorporating confidential Aventis information into the applications leading to the issuance of the '191 patent;

(C) a judgment that Introgen shall pay all appropriate damages caused by the breach of the collaboration agreement;

(D) such other and further relief as the Court may deem just and equitable.

DEMAND FOR JURY TRIAL

Aventis demands a trial by jury of all issues so triable.

Respectfully submitted,

Date: June 29, 2001

By: Christine M. Hansen

Christine M. Hansen (#3098)
Connolly Bove Lodge & Hutz LLP
1220 Market Street
Wilmington, Delaware 19801
Telephone: (302) 658-9141
Facsimile: (302) 658-5614

Of counsel:

Paul H. Berghoff
Curt J. Whitenack
McDonnell Boehnen Hulbert & Berghoff
300 S. Wacker Drive, Suite 3200
Chicago, Illinois 60606
Telephone: (312) 913-0001
Facsimile: (312) 913-0002